



# CASE REPORTS

## Systemic Moniliasis

### Report of a Case

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THE INTRODUCTION of chemotherapeutic agents and antibiotics has proved to be a mixed blessing. The miraculous cures of formerly fatal diseases as well as of the less spectacular nonfatal but incapacitating diseases, has been accompanied by a significant number of complications, such as all types of allergic reactions, kidney damage, agranulocytosis, the emergence of resistant organisms and—as in the case here reported—the overgrowth of nonsusceptible organisms.

### REPORT OF A CASE

A two-year-old white boy was admitted to the Communicable Disease Unit of the Los Angeles County General Hospital on March 10, 1954, with complaint of stiffness of the neck of one day's duration. Headache, lethargy and a fever of 103° F. had been noted on the night prior to admission. The patient had had no other recent illness.

At the time of admittance the temperature was 103° F., the pulse rate 160 and respirations 40 per minute. The patient was well-developed and well-nourished. He was lethargic and irritable. The left tympanic membrane was dull, the posterior pharynx reddened, the neck severely stiff, and reflexes hypoactive but equal.

The cerebrospinal fluid was cloudy and the leukocyte content was 3,400 per cu. mm. (differential not noted). The pressure of spinal fluid was not determined. Gram-positive rods were observed in a specimen of the fluid sediment, and *Hemophilus influenza*, type B, grew on a culture of the material. The hemoglobin content of the blood was 11 gm. per 100 cc. and the leukocyte content was 3,300 per cu. mm. with 72 per cent neutrophils.

Penicillin was given intravenously (averaging 30 million units per day for four days), chloramphenicol (1.5 gm. per day after 3 gm. on the first day) and sulfisomidine (Elkosin®) intravenously and subcutaneously 6 to 9 gm. per day. General supportive measures were carried out—administration of

adrenal cortical extract, sedation and gastric suction. On the fifth day of this therapy the spinal fluid cell content was 40 per cu. mm. with 1 neutrophil. Penicillin and chloramphenicol then were discontinued. On the ninth day, phlebitis and an infection at the site of the intravenous infusions were noted. The leukocyte content was 28,500 per cu. mm. of blood, with 78 per cent neutrophils. The general clinical condition of the patient had remained poor and the possibility of loculation of the meningeal infection was considered. On the twelfth hospital day the cerebrospinal fluid contained 561 cells per cu. mm., 20 per cent neutrophils. This and a continuing elevation of the leukocyte content in the blood seemed to indicate that the infection was not under control, and streptomycin (1 gm. per day) and Alexander's serum\* (50 mg. per day for two days) were given. In addition, streptokinase-streptodornase (Veridase®) was instilled intraspinally, 2,500 units three times daily, in an attempt to break up the suspected loculations. On the 13th day a combination of sulfadiazine and sulfamerazine (a total of 6 gm. per day) replaced sulfisomidine because the supply of that drug had been exhausted. On the 15th day chloramphenicol was again started, but it was again discontinued after two days. At about this time, a culture of blood and a culture of material taken from the infected area about the site of venipuncture grew *Candida albicans*. On the 16th day administration of a saturate solution of potassium iodide was started, beginning with five drops three times daily and increasing so that a maximum of 60 drops three times daily was reached on the 27th day and was maintained until the 42nd day. On the 16th day it was also noted that the cerebrospinal fluid showed 548 cells per cu. mm., 2 of them neutrophils. Also there was a decrease in the sugar content of the fluid. Because of the decreased sugar, it was felt that the phenomena were more than just a reaction to Veridase, and were caused by a growth of organisms. For this reason, sulfadiazine and sulfamerazine were continued. The cell content of the cerebrospinal fluid then decreased and the sugar content returned to normal. The number of leukocytes in the blood also decreased. The sulfa drugs were discontinued on the 22nd day. On the 24th day the patient was found to have several abscesses on the lateral aspect of both thighs. These were surgically opened and cleansed,

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Submitted September 26, 1955.

\*Hyper-immune sera for *Hemophilus influenzae*, type B.

and drains were inserted. Cultures of material from the abscesses grew *Candida albicans* on two occasions. No organisms grew on further cultures of the blood, but monilia grew on a culture of urine on the 22nd day. Surprisingly, no monilia were recovered from the feces. After the 27th day all cultures were sterile. The patient continued to have a low grade fever intermittently until the 45th day, and thereafter seemed entirely well. In fact, he began to look and act better about a week after the abscesses were drained. The patient continued to do well and was discharged on the 56th hospital day with no demonstrable residual effect.

An x-ray film taken on the 23rd day of illness showed a "haze over the left upper lung field." An electroencephalogram was normal. After the growth of *Hemophilus influenza* on the first culture of cerebrospinal fluid, all subsequent ones were sterile.

When observed one month after discharge, it was noted that, except for "bronchitis," which had been treated by another physician, the patient was doing very well. His mother had noted a questionable wide gait, but this was apparently not striking.

#### DISCUSSION

A rising incidence of mycotic infections, both primary and secondary, has been noted. The monilias have been the most common offender and their cultural characteristics have been typical, but growth occurs in a much shorter time than usual. They have been found in increasing numbers in their usual habitat (mouth, throat, sputum, and vagina) as well as in the urinary tract. There appears to be a consistent concomitant in most cases: Usually there was notation that more than one antibiotic had been administered. This may be a contributing factor or it may be merely coincidental with multiple antibiotic treatment, which is the rule in present day therapy. The majority of the disseminated monilia infections have been fatal and monilia lesions have been observed in most of the organs at autopsy.

Sharp,<sup>6</sup> in England, observed in study of a group of 174 pneumonia patients that the proportion of cases in which cultures grew monilia was higher when terramycin was the therapeutic agent than when sulfadiazine was used. Cultures of material from the throat, which were positive for monilia in 16 per cent of cases upon admission were positive in 42 per cent after five days of treatment. The corresponding data for cultures of sputum were 32 per cent and 61 per cent, for rectal cultures were 0 and 59 per cent. None of the patients had symptoms and the incidence of positive cultures decreased when the antibiotic was stopped.

A patient reported upon by Browne<sup>2</sup> was under treatment with succinylsulfathiazole, diodoquin, emetine, and penicillin for amebiasis and liver abscess. He was treated with potassium iodide and gentian violet and recovered. Brown and co-workers<sup>1</sup> reported five fatal cases of fungus infection, in all of which the patient received multiple antibiotics for

some type of primary infectious process. In all of the cases except one, cultures of the blood were positive for monilia. The monilia infection was accompanied by disseminated aspergillosis and agranulocytosis after penicillin and chloramphenicol therapy. Huppert<sup>3</sup> reviewed the various theories that have been postulated for the increased incidence of candidosis as a complication of antibiotic treatment. One theory is that of "suppression with substitution"—that is, that administration of antibiotics upsets the equilibrium of normal flora, permitting resistant species to increase. Another is that the normal flora supply certain nutritional requirements to the host and that disturbance of the normal flora results in a nutritional effect upon the integrity of the mucous membrane, making it penetrable by microorganisms not usually able to pass through it. A third theory is that some antibiotics directly stimulate the growth and increase the virulence of *Candida albicans*. Other studies have shown that Aureomycin stimulated the *in vitro* growth of *Candida albicans* significantly, while penicillin, chloramphenicol, streptomycin, and terramycin did not. Huppert and co-workers<sup>3</sup> cited the work of McVay and Sprund in 1951, who showed that cultures of oral, vaginal and rectal material were positive for *Candida albicans* in 63 per cent of cases after Aureomycin was given, whereas none was positive before. This phenomenon has been observed with most antibiotics administered orally or parenterally.

In the case of *Hemophilus influenza* meningitis reported herein, many drugs were given, including penicillin, chloramphenicol, sulfadiazine, sulfamerazine, sulfisomidine and streptomycin. The treatment was prolonged because of the apparent relapse of meningitis. The diagnosis of disseminated moniliasis in this patient was confirmed by multiple cultures of materials from various sites (blood, urine and subcutaneous abscess). The patient had no sequelae. The role of potassium iodide must be assessed. Certainly the stopping of antibiotics and drainage of the abscesses contributed to the recovery.

#### SUMMARY

In a case of *Hemophilus influenza* (type B) meningitis treated with multiple antibiotics and sulfa drugs, systemic moniliasis developed during antibiotic therapy. The patient recovered after surgical drainage of subcutaneous abscesses, discontinuation of the antibiotics and intensive treatment with a saturated solution of potassium iodide. A portion of the literature on the subject of moniliasis is discussed. The cause of systemic monilia has not been established at this time.

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## Nitrofurantoin in Treatment of Coliform Bacteremia

### Report of a Case

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THE USE OF FURADANTIN® (nitrofurantoin, N. N. R.), one of the group of antibacterial nitrofurans, has been established in the treatment of resistant strains of certain gram-positive and gram-negative bacterial infections of the urinary tract. The general literature was reviewed by Trafton and co-workers<sup>9</sup> but the treatment of bacteremia was not included. In a medical research forum at the New York Academy of Medicine, Friedgood and Ripstein<sup>2</sup> briefly mentioned six cases of *B. proteus* septicemia successfully treated with Furadantin but gave no details.

Consequently, reports to date do not deal with bacteremia but rather with infections limited to the urinary tract. The purpose of the present communication is to report in detail the successful treatment of a case of persistent bacteremia due to *E. coli*, the focus of which was presumably the urinary tract, and to discuss the possible relationship of the disease in this case to the administration of adrenocortical hormones. In this particular case, bacteremia was not cleared by administration of streptomycin in combination with certain of the broad spectrum antibiotics.

### CASE REPORT

A 63-year old man had sudden onset of a shaking chill and fever, followed shortly by nausea, vomiting and prostration. Chills continued, prostration increased and the patient was admitted to hospital at night, six hours after the onset of symptoms. The patient had had mild dysuria and low backache for two days before the acute illness developed. Upon physical examination the patient was observed to be prostrated and the skin was flushed and dry. The temperature was 101° F., the pulse rate 104 and blood pressure 140/75 mm. of mercury. Severe shaking chills continued and at 1 o'clock in the morning, following an unusually heavy chill, the

temperature was 107° F. (This temperature was confirmed.) At that time a specimen of blood was obtained for culture, and 600,000 units of aqueous procaine penicillin then was administered intramuscularly.

The following morning, the temperature was 103.2° F., the pulse rate 112 and blood pressure 74/50 mm. of mercury. The patient was lethargic but could be aroused. The skin was flushed and dry but without eruption or petechiae. Pulses were equal, rapid and regular. Heart sounds were somewhat distant but there were no murmurs. The lungs were clear. The abdomen was flat and no masses were palpated. Slight tenderness was noted in the right upper quadrant.

The urine was turbid with acid reaction, specific gravity of 1.018, a 1 plus reaction for albumin and a trace of sugar. Acetone and diacetic reactions were negative. Upon microscopic examination of centrifuged sediment, a solid field of erythrocytes and 10 to 15 leukocytes per high power field were noted. A few gram-negative rods were seen. There was a heavy growth of *E. coli* on a culture of the urine.

Erythrocytes numbered 4,250,000 per cu. mm. and the hemoglobin content was 13.2 gm. per 100 cc. Leukocytes numbered 7,650 per cu. mm.—40 per cent stab neutrophils, 42 per cent adult neutrophils, 7 per cent lymphocytes, and 1 per cent monocytes. There was pronounced toxic granulation of the neutrophils.

In view of the urinary abnormalities and the relative leukopenia with a pronounced shift to the left, it appeared clear that the patient had bacteremia from a focus probably in the urinary tract. Accordingly, 500 mg. of chlortetracycline was administered intravenously without delay and a similar dose was given six hours later. The hypotension and obvious apathy suggested the possibility of impending shock, perhaps due to adrenal cortical damage, and 40 cc. of adrenal cortical extract was given intravenously over an 8-hour period. Cortisone was begun in a dosage of 200 mg. daily, given by mouth at 6-hour intervals.

Early in the afternoon of the day following admittance, a report was received that gram-negative bacilli grew on a culture of blood. A combination of oxytetracycline and streptomycin was begun in total daily doses of 1.5 gm. and 4.0 gm. respectively, the latter intramuscularly.

While arrangements were being made for the administration of adrenal cortical extract, the blood pressure decreased to 68/50 mm. of mercury. After the administration of 10 cc. of adrenal cortical extract, the pressure rose to 82/50 mm. and by the time of administration of the second 10 cc. dose one hour later, it was 98/56 mm.

Data on the subsequent course are given in Chart 1. Daily blood cultures were obtained, the blood pressure was carefully observed, and leukocyte and differential counts were made daily. The blood pressure rose to 130/78 mm. of mercury the day

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Submitted November 11, 1955.